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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| 09/834,307 | 04/12/2001 | Richard J. Whitbourne | P-1663-1 | 3036 |

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| EXAMINER | |
|---|---|
| BENNETT, RACHEL M | |

| ART UNIT | PAPER NUMBER |
|---|---|
| 1615 | 10 |

DATE MAILED: 03/31/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 09/834,307 | WHITBOURNE ET AL. | |
| | Examin r | Art Unit | |
| | Rachel M. Bennett | 1615 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondenc address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *24 December 2002* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1-22* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-22* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

**Priority under 35 U.S.C. §§ 119 and 120**

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

**Attachment(s)**

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:



[redacted]

## DETAILED ACTION

The examiner acknowledges receipt of Amendment A filed 12/24/02.

### *Specification*

### *Claim Rejections - 35 USC § 102*

1. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

2. Claims 1-2, 9-10, 18 are rejected under 35 U.S.C. 102(b) as being anticipated by Whitbourne et al. (US 5525348).

The instant application is drawn to a medicated device comprising a scaffold member, a polymeric coating on the member and the polymeric coating containing at least one therapeutic agent.

Whitbourne et al. disclose anti-thrombogenic, and/or anti-microbial and/or pharmaceutical compositions containing heparin and/or antibiotics and/or other pharmaceutical agents which may be reacted with quaternary ammonium components or other ionic surfactants and bound with water-insoluble polymers are disclosed. See Abstract. Whitbourne et al. provide novel anti-thrombogenic/polymer/heparin compound compositions or mixtures which prevent blood clotting for a relatively long period of time (over one month), and which have the same high degree of anti-thrombogenic characteristics as the non-polymerized heparin-quaternary ammonium compounds, and thus provide excellent properties for use as medical materials for coatings on artificial blood vessels, catheters, artificial hearts, artificial kidneys,

etc. Pharmaceutical agents that are not reacted with ionic surfactants may also be used, providing that they have the appropriate solubility profile namely that they are soluble in organic solvents. They may also contain some hydrophilic polymers. A single polymer or mixture(s) of different polymers may be used. Typical examples of polymers suitable for use with the present invention are as follows: Water insoluble cellulose esters such as cellulose acetate, cellulose acetate butyrate, cellulose acetate propionate, and cellulose nitrate; polyurethane resins including polyether and polyester grades.

Whitborune claims: 1) A device comprising: a substrate, and a coating composition comprising a pharmaceutical agent in a concentration of from about 0.5% to about 99.5% by weight and a water-insoluble cellulose ester polymer, the coating composition being resistant to removal and having pharmaceutical activity under physiological conditions. 3) The device of claim 1 wherein the water insoluble cellulose ester polymer is selected from the group consisting of cellulose acetate propionate, cellulose acetate, cellulose acetate butyrate, cellulose nitrate, cellulose acetate phthalate, and mixtures thereof. 5) The device of claim 1 wherein the pharmaceutical agent is selected from the group consisting of an antithrombogenic material, an antibiotic material, an anticancer material, and mixtures thereof. 10) The device of claim 1 wherein the pharmaceutical agent is ionic and the coating composition further comprises a surfactant which is capable of complexing the pharmaceutical agent. 14) The device of claim 1, in which the device is selected from the group consisting of a catheter, a needle, a fluid drainage device, a suction device, aspiration device, an artificial blood vessel, an artificial heart, and an artificial kidney. 31) The device of claim 1, in which the coating further comprises polyvinylpyrrolidone. Whitbourne et al. also claim: 37) A coated article comprising: a

substrate; and a coating comprising a pharmaceutical agent in a concentration of from about 0.5% to about 99.5% by weight, and a water-insoluble cellulose ester polymer, the pharmaceutical agent being entrained in the cellulose ester polymer in such a way as to be gradually released under physiological conditions, to provide effective concentrations of the pharmaceutical agent at the surface of the coating over a useful period, and the coating being adherent to the substrate and essentially water-insoluble. 39) The coated article of claim 37, in which the coating further comprises polyvinylpyrrolidone. 40) The coated article of claim 37, the coating having inner and outer layers, the inner layer adhering to the substrate and comprising a cellulose ester, and the outer layer having an exposed outer surface and comprising a cellulose ester and a pharmaceutical agent. 41) The coated article of claim 40, the inner layer comprising cellulose ester and polyurethane, and the outer layer comprising cellulose ester, polyvinylpyrrolidone, and a pharmaceutical agent.

Whitbourne et al. disclose a medicated device comprising a scaffold, a polymeric coating and at least one therapeutic agent. Therefore, these claims are anticipated.

***Claim Rejections - 35 USC § 103***

3. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

4. Claims 1-5, 9-10, 18 are rejected under 35 U.S.C. 103(a) as being unpatentable over Whitbourne et al. (US 5525348).

Whitbourne et al., as disclosed above, teaches coating compositions comprising pharmaceutical agents such as anti-thrombogenic, and/or antimicrobial and/or pharmaceutical compositions containing heparin and/or antibiotics mixed with polymers (see abstract). Whitbourne does not teach the device to comprise at least 5 to 500 μg of at least one therapeutic agent.

The instant claims differ from the reference by reciting various doses of the active ingredient(s). However, the preparation of various pharmaceutical formulations having various amounts of the active agent is with in the level of skill of one of ordinary skill in the art at the time of the invention. It has also been held that the mere selection of proportions and ranges is not patentable absent a showing of criticality. In re Russell, 439 F. 2nd 1228, 169 USPQ 426 (CCPA 1971). Thus, absent unexpected results, it is the position of the examiner that it would have been obvious to one of ordinary skill in the art at the time the invention was made to have modified the amount of therapeutic agent.

5. Claims 1-22 are rejected under 35 U.S.C. 103(a) as being unpatentable over Whitbourne et al. (US 5525348), and further in view of Whitbourne (US 6306176).

Whitbourne et al., as disclosed above, teaches coating compositions comprising pharmaceutical agents such as anti-thrombogenic, and/or antimicrobial and/or pharmaceutical compositions containing heparin and/or antibiotics mixed with polymers (see abstract). Whitbourne does not teach the device to comprise an acrylate polymer and PVP/VA copolymer in a weight ratio in the range of 1.5:1 to 7:1 or the polymeric coating comprises a major portion of one or more hydrophilic polymer materials and a minor portion of one or more hydrophobic polymeric materials.

Whitbourne '176 discloses bonding layers for medical device surface coatings. The coatings may be applied to inert metal or plastic surfaces of medical devices such as needles, guide wires, catheters, surgical instruments, equipment for endoscopy, wires, stents, angioplasty balloons, wound drains, arteriovenous shunts, gastroenteric tubes, urethral inserts, laparoscopic equipment, pellets, and implants. It is an object of the present invention to provide materials which can be applied within layers directly on medical device surfaces on which it is difficult to achieve coating adhesion, and which allow layers to be applied over them to enhance performance and biocompatibility of such devices. Also discloses are methods for preparing such medical instruments such as guide wires, catheters, drainage tubes, feeding tubes, and other devices which are used in contact with human tissues and fluids, with surfaces that show enhanced biocompatability and may become very lubricious when contacted by body fluids. Such devices which contain substances which combat infections, blood clots, inflammation, and other disorders that may result from in vitro placement and use of such medical devices. Classes of polymers, which may be used in the coating, include acrylic polymers and copolymers, vinyl polymers and copolymers such as polyvinylpyrrolidone and polyvinylpyrrolidone polyvinyl acetate copolymers.

Absent unexpected results, it would have been obvious to one of ordinary skill in the art at the time the invention was made to have modified the composition of Whitbourne ('348) by substituting PVA/VA for PVP as taught by Whitbourne ('176) because of the expectation of obtaining similar results without undue experimentation. Whitbourne ('176) discloses both PVP and PVA/VA may be used in a coating layer on a medical device. Therefore, it would be obvious to substitute PVP/VA for PVP and determine a suitable ratio of PVP/VA to an acrylate

polymer (surfactant) in order to obtain the desired release rate of the active ingredient. Furthermore, absent unexpected results, it would have been obvious to one of ordinary skill in the art at the time the invention was made to have modified the composition of '348 by modifying the polymeric coating to comprise a major portion of one or more hydrophilic polymer materials and a minor portion of one or more hydrophobic polymeric materials in order to obtain a device with surfaces that show enhanced biocompatability and a desired release rate of the pharmaceutical agent as taught by '176.

***Response to Arguments***

6. Applicant's arguments filed 12/24/02 have been fully considered but they are not persuasive.

*Rejection -102(b)*

Applicants argue '348 does not teach or suggest the use of a substrate as defined in the specification. The examiner refers to '348 wherein medical materials for coating include artificial blood vessels and catheters. Therefore, the limitation of "scaffold" is met by '348.

*Rejection 103(a)*

7. Applicant's arguments filed 12/24/02 have been fully considered but they are not persuasive. Applicants argue'348 does not disclose does not teach or suggest a substrate in a medically coated device. Furthermore, Applicant argue '348 and '176 contain agents in prophylactic amounts to prevent pathologies at the surface of the device, not in therapeutic amounts and that neither of the references teach the relative hydrophilic-hydrophobic proportions necessary to permit the desired loading of therapeutic agent in the coating.

The examiner refers to both '348 and '176 wherein both hydrophilic and hydrophobic polymers are used to coat medical devices for sustained release. '348 discloses a pharmaceutical agent is released over a relatively long period of time (over one month). Therefore, it is the position of the examiner it would have been obvious to one of ordinary skill in the art at the time the invention was made to have modified the coatings taught by both '348 and '176 to determine the ideal ratio of hydrophilic polymer to hydrophobic polymer in order to achieve the desired release rate of the pharmaceutical agent. Furthermore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to have modified the amount of therapeutic agent depending on the specific agent, patient population and the condition being treated.

***Conclusion***

8. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

*Correspondence*

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Rachel M. Bennett whose telephone number is (703) 308-8779. The examiner can normally be reached on Monday through Friday, 8:00 A.M. to 4:30 P.M..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Thurman K. Page can be reached on (703) 308-2927. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 305-3592 for regular communications and (703) 309-7924 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-1234.

R. Bennett
March 28, 2003

THURMAN K. PAGE
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600